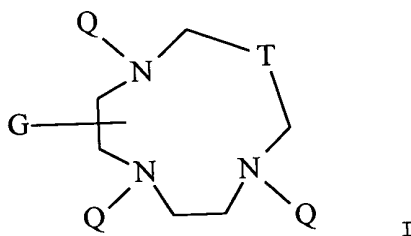


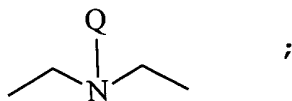
What is claimed is:

1. An Actinium-225 complex comprising a functionalized
polyazamacrocyclic chelant compound of the formula I,
hereinbelow:

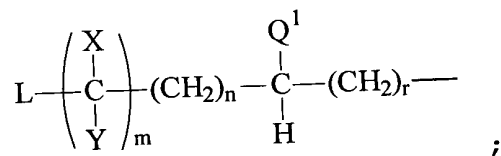


wherein:

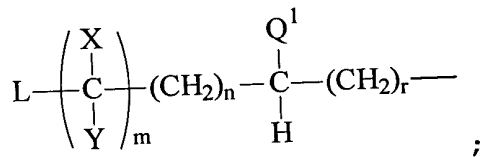
T is



G is independently hydrogen or



each Q is independently hydrogen, $(CHR^5)_p CO_2R$ or
 $(CHR^5)_p PO_3R^6R^7$ or



Q^1 is hydrogen, $(CHR^5)_w CO_2R$ or $(CHR^5)_w PO_3R^6R^7$;

each R is independently hydrogen, benzyl or C_1 - C_4 alkyl;

R^6 and R^7 are independently H, C_1 - C_6 alkyl or $(C_1$ - C_2

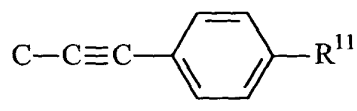
alkyl)phenyl;

each R^5 is independently hydrogen; C_1 - C_4 alkyl or

$(C_1$ - C_2 alkyl)phenyl;

with the proviso that at least two of the sum of Q and Q¹ must be other than hydrogen;

A is CH, N, C-Br, C-Cl, C-SO₃H, C-OR⁸, C-OR⁹N⁺-R¹⁰X⁻, or



5 Z and Z¹ independently are CH, N, C-SO₃H, N⁺-R¹⁰X⁻, C-CH₂-OR⁸ or C-C(O)-R¹¹;

R⁸ is H, C₁-C₅ alkyl, benzyl, or benzyl substituted with at least one R¹²;

R⁹ is C₁-C₁₆ alkylamino;

10 R¹⁰ is C₁-C₁₆ alkyl, benzyl, or benzyl substituted with at least one R¹²;

R¹¹ is -O-(C₁-C₃ alkyl), OH or NHR¹³;

R¹² is H, NO₂, NH₂, isothiocyanato, semicarbazido, thiosemicarbazido, maleimido, bromoacetamido or
15 carboxyl;

R¹³ is C₁-C₅ alkyl;

X and Y are each independently hydrogen or may be taken with an adjacent X and Y to form an additional carbon-carbon bond;

20 n is 0 or 1;

m is an integer from 0 to 10 inclusive;

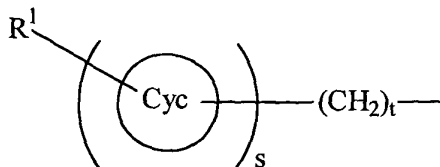
p is 1 or 2;

r is 0 or 1;

w is 0 or 1;

25 with the proviso that n is only 1 when X and/or Y form an additional carbon-carbon bond, and the sum of r and w is 0 or 1;

L is a linker/spacer group covalently bonded to, and replaces one hydrogen atom of one of the carbon atoms
30 to which it is joined, said linker/spacer group being represented by the formula



wherein:

s is an integer of 0 or 1;

5 t is an integer of 0 to 20 inclusive;

R¹ is H or an electrophilic or nucleophilic moiety which allows for covalent attachment to a biological carrier, or synthetic linker which can be attached to a biological carrier, or precursor thereof; and

10 Cyc represents a cyclic aliphatic moiety, aromatic moiety, aliphatic heterocyclic moiety, or aromatic heterocyclic moiety, each of said moieties optionally substituted with one or more groups which do not interfere with binding to a biological carrier;

15 with the proviso that when R¹ is H, the linkage to the biological carrier is through one of Q or Q¹; and with the proviso that when R¹ is other than H, at least one of Q and Q¹ must be (CHR⁵)_pPO₃R⁶R⁷; and with further proviso that when Q is (CHR⁵)_pCO₂R, Q¹ is (CHR⁵)_wCO₂R, R is H, R⁵ is H, and R¹ is H, then the sum of m, n, p, r, s, t, and w is greater than 1;

20

or pharmaceutically acceptable salt thereof; complexed with ²²⁵Ac.

- 25 2. A conjugate comprising the complex of Claim 1 covalently attached to a biological carrier.
3. The conjugate according to Claim 2 wherein the biological carrier is a protein, antibody, antibody fragment, hormone, peptide, growth factor, antigen or
- 30 hapten.

- 5



10

$$(\text{CHR}^5)_p\text{PO}_3\text{R}^6\text{R}^7 \text{ or}$$


Q^1 is hydrogen, $(CHR^5)_wCO_2R$ or $(CHR^5)_wPO_3R^6R^7$;

15

(C₁-C₂ alkyl)phenyl;

20

with an adjacent X and Y to form an additional carbon-carbon bond;

25

m is an integer from 0 to 10 inclusive;

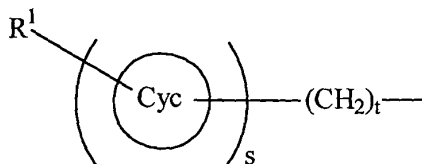
p is 1 or 2;

r is 0 or 1;

w is 0 or 1;

5 with the proviso that n is only 1 when X and/or Y form an additional carbon-carbon bond, and the sum of r and w is 0 or 1;

L is a linker/spacer group covalently bonded to, and replaces one hydrogen atom of one of the carbon atoms to which it is joined, said linker/spacer group being
10 represented by the formula



wherein:

15 s is an integer of 0 or 1;

t is an integer of 0 to 20 inclusive;

R¹ is H or an electrophilic or nucleophilic moiety which allows for covalent attachment to a biological carrier, or synthetic linker which can be attached to a
20 biological carrier, or precursor thereof; and

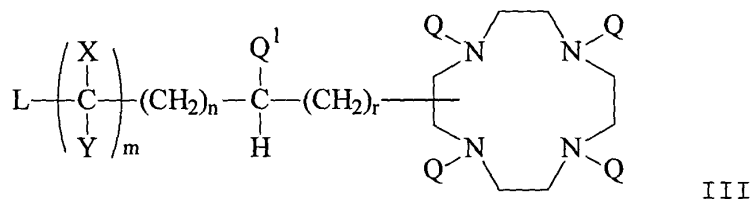
Cyc represents a cyclic aliphatic moiety, aromatic moiety, aliphatic heterocyclic moiety, or aromatic heterocyclic moiety, each of said moieties optionally substituted with one or more groups which do not
25 interfere with binding to a biological carrier;

with the proviso that when R¹ is H, the linkage to the biological carrier is through one of Q or Q¹; and with the proviso that when R¹ is other than H, at least one of Q and Q¹ must be (CHR⁵)_pPO₃R⁶R⁷; and with further
30 proviso that when Q is (CHR⁵)_pCO₂R, Q¹ is (CHR⁵)_wCO₂R, R

is H, R^5 is H, and R^1 is H, then the sum of m, n, p, r, s, t, and w is greater than 1;

or pharmaceutically acceptable salt thereof.

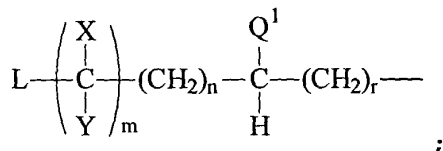
6. The complex according to Claim 1 wherein the
5 functionalized chelant is a compound of formula III



10

wherein:

each Q is independently hydrogen, $(\text{CHR}^5)_p\text{CO}_2\text{R}$ or $(\text{CHR}^5)_p\text{PO}_3\text{R}^6\text{R}^7$ or



- 15 Q^1 is hydrogen, $(\text{CHR}^5)_w\text{CO}_2\text{R}$ or $(\text{CHR}^5)_w\text{PO}_3\text{R}^6\text{R}^7$;
each R is independently hydrogen, benzyl or $\text{C}_1\text{-C}_4$ alkyl;
 R^6 and R^7 are independently H, $\text{C}_1\text{-C}_6$ alkyl or $(\text{C}_1\text{-C}_2$
alkyl)phenyl;
each R^5 is independently hydrogen; $\text{C}_1\text{-C}_4$ alkyl or
20 $(\text{C}_1\text{-C}_2$ alkyl)phenyl;
with the proviso that at least two of the sum of Q and
 Q^1 must be other than hydrogen;
X and Y are each independently hydrogen or may be taken
with an adjacent X and Y to form an additional carbon-
25 carbon bond;
n is 0 or 1;
m is an integer from 0 to 10 inclusive;

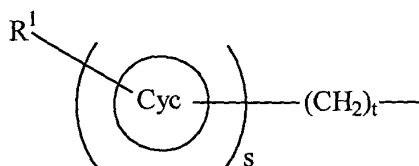
p is 1 or 2;

r is 0 or 1;

w is 0 or 1;

with the proviso that n is only 1 when X and/or Y form
 5 an additional carbon-carbon bond, and the sum of r and
 w is 0 or 1;

L is a linker/spacer group covalently bonded to, and
 replaces one hydrogen atom of one of the carbon atoms
 to which it is joined, said linker/spacer group being
 10 represented by the formula



wherein:

15 s is an integer of 0 or 1;

t is an integer of 0 to 20 inclusive;

R¹ is H or an electrophilic or nucleophilic moiety which
 allows for covalent attachment to a biological carrier,
 or synthetic linker which can be attached to a
 20 biological carrier, or precursor thereof; and

Cyc represents a cyclic aliphatic moiety, aromatic
 moiety, aliphatic heterocyclic moiety, or aromatic
 heterocyclic moiety, each of said moieties optionally
 substituted with one or more groups which do not
 25 interfere with binding to a biological carrier;

with the proviso that when R¹ is H, the linkage to the
 biological carrier is through one of Q or Q¹; and with
 the proviso that when R¹ is other than H, at least one
 of Q and Q¹ must be (CHR⁵)_pPO₃R⁶R⁷; and with further
 30 proviso that when Q is (CHR⁵)_pCO₂R, Q¹ is (CHR⁵)_wCO₂R, R

is H, R^5 is H, and R^1 is H, then the sum of m, n, p, r, s, t, and w is greater than 1;

or a pharmaceutically acceptable salt thereof.

- 5 7. A conjugate according to Claim 2 comprising the ^{225}Ac complex of DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid) covalently attached via amide linkage to a biological carrier.
- 10 8. A conjugate according to Claim 2 comprising the ^{225}Ac complex of 2-(p-isothiocyanatobenzyl)-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid covalently attached to a biological carrier.
9. A pharmaceutical formulation comprising the ^{225}Ac conjugate of Claim 2 and a pharmaceutically acceptable carrier.
- 15 10. The formulation of Claim 9 wherein the pharmaceutically acceptable carrier is a liquid.
11. A method of therapeutic treatment of a mammal having cancer which comprises administering to said mammal a therapeutically effective amount of the formulation of
20 Claim 9.